REMARKS

1. Amendments to the Claims

Claims 1-5, 7-10, 12-15, 17-22, 25-27, 29, 32, 34-43, and 46-48 are pending. Claims 30 and 49 are herein cancelled. Claims 1, 17, 26, 29, and 48 are herein amended. Claims 1, 29, and 48 are supported by the Specification at page 9, lines 35-38. Claims 17 and 26 are amended support is found in the Specification at page 10, lines 15-17.

No new matter has been added.

2. Objections to the Claims

a. Claims 30 and 49

The Examiner objects to claims 30 and 49 as including in the alternative the subject matter of the non-elected invention, i.e., prior to surgery. This objection is based on the restriction requirement. Applicants have cancelled claims 30 and 49. Applicants request that the objection be withdrawn.

b. Claims 17, 26, 30 and 31

The Examiner objects to claims 17, 26, and 30-31 as drawn to non-elected subject matter. Applicants have amended claims 17 and 26 to recite only the elected subject matter and cancelled claims 30 and 31. Applicants request that the objection be withdrawn.

3. Indefiniteness

The Examiner rejects claims 1-5, 7-10, 12-15, 17-22, 25-27, 29-32, 34-43, and 46-49 under 35 U.S.C. § 112, second paragraph, as indefinite. Applicants have returned the claims to their format from prior to the amendment of December 8, 2008. As the Examiner had not made a rejection in the Office Action of August 7, 2008, Applicants submit that the claims are clear. Applicants request that the rejection be withdrawn.

4. Novelty

The Examiner maintains the rejection of claims 1-5, 7-8, 10, 12-15, 18-19, 22, 46, 48, and 49 under 35 U.S.C. § 102(b) as anticipated by U.S. Patent 5,716,595 (hereinafter Goldenberg). The Examiner maintains the rejection of claims 1-5, 7-8, 10-12-15, 18-19, 48, and 49, under 35 U.S.C. § 102 (b) as anticipated by U.S. Patent 6,107,102 (Ferrari). Applicants respectfully traverse.

Applicants submit that Goldenberg and Ferrari do not anticipate the present invention because the antibodies of Goldenberg and Ferrari are antibodies which are tied to a fluor for imaging tumors or for the delivery of drugs or microdevices, and as such, are functionally impaired when administered as a method of treatment.

Applicants submit that Goldenberg discloses antibodies for targeting tumors which are labeled with a dye, and an isotope or a drug. (Goldenberg, col. 9, lines 20-24). Ferrari discloses antibodies bound to a microdevice. The antibodies tied to the microdevices may be considered an immobilized therapeutic agent. (Ferrari, col. 13, lines 46-48).

However, both antibody modifications lead to an impairment of antibody activity. Such impairment is defined by either the antigen binding activity or the effector function mediated by the Fc part. Both functions are necessary to be functionally active according to the present invention in order to both bind the tumor cells and then to clear the tumor cells by action of the effector function. As described in the Specification, the present antibodies lead to the reduction of tumor cells so as to prevent their dissemination as far as possible, such that the disseminated cells are attacked. (Specification, page 14, lines 19-25, page 12, lines 23-28).

Since the antibodies of the prior art are bound or labeled, they likely use one of three strategies. (See Attached Antibody Labeling Overview).

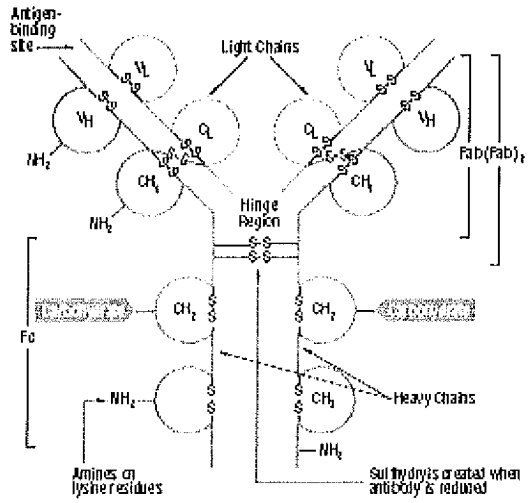

Figure 24. Antibody labeling sites.

The most common target for antibody labeling is primary amines, which are found primarily on lysine residues. They are abundant, widely distributed, easily modified, and are located on the surface of the antibody. However, this labeling strategy often results in a significant decrease in the antigen-binding activity of the antibody. This decrease may be particularly pronounced when working with monoclonal antibodies or when multiple labels are attached to the antibody.

The second common target for labeling antibodies is carbohydrate moieties, because antibodies are often significantly glycosylated. Because the glycosylation sites are predominantly found on the Fc portion of the antibody, they can often (not always) be modified without significantly reducing the antigen-binding capacity. In contrast, the ability to mediate effector functions via the Fc part will be influenced by lableling. Labeling carbohydrates requires more steps than labeling amines because the carbohydrates must first be oxidized (the whole antibody is subjected to this process that might also result in oxidizing certain amino acids – e.g., methionine – that will affect the mAb properties) to create reactive aldehydes; however, it generally results in antibody conjugates with high activity.

The third common target is sulfhydryls that exist in proteins under reducing conditions, but more often are found in oxidized form as disulfide bonds. Disulfide bonds are important contributors to antibody structure as they participate in the tertiary structure of each subunit, covalently

connecting the heavy and light chains and connecting the two halves of an antibody in the hinge region. These disulfides in the hinge region are the primary target for sulhydryl labeling of an antibody because they are easily reduced to sulfhydryls, splitting the antibody into monovalent halves (rIgG) without damaging the antigen-binding sites (but resulting in a loss of Fc mediated effector functions).

Each of these labeling methods poses the threat of decreasing the efficacy of the antibody- either by influencing the binding of the antibody to the target cells or by influencing the effector functions. A functional Fc part is required for binding to CD16 to mediate target cell lysis. This principle also applies for attaching microdevices as disclosed by Ferrari et al.

Thus, Applicants submit that the feature "whereby immunocomplexing of tumor cells within the scope of the surgical intervention inhibits dissemination of tumor cells" is not disclosed by Goldenberg or Ferrari, since neither reference uses their antibodies as active agents for therapy, and do not demonstrate therapeutic activity in the absence of these additive agents. Instead the antibodies are used as a marker or a transporter of other agents to the site of the tumor. Because of these attachments, the antibody would not necessarily have any therapeutic activity, thus the activity is not inherently present. Accordingly, Applicants submit that neither Goldenberg nor Ferrari anticipate the claimed invention.

Even further, a mild therapeutic activity does not equate to the therapeutic activity required to prevent dissemination of tumor cells during surgical intervention. Dissemination of tumor cells during surgery is a violent mechanical detachment of a large number of tumor cells compared to dissemination during growth or metastases. Only highly effective agents, which can neutralize tumor cells in a short period of time are suitable for the claimed procedure. Labels are clearly contra-productive. Microdevices with chemotherapeutic agents also do not allow a quick attach of the tumors, and do not provide the tumor cell clearance achieved by the claimed antibodies with their native Fc mediated effector function.

Thus, Applicants submit that neither Goldenberg nor Ferrari anticipate the claimed invention.

5. Obviousness

The obviousness rejections are based on either Goldenberg or Ferrari in combination with some arrangement of Schlimok, Crisan, and U.S. Patent 5,792,456 ('456). Specifically, the Examiner rejects claims 1, 9, 17, 20, 25-27, 29-32, 35-40, 43, and 47 as unpatentable over Goldenberg in view of Sclimok and Crisan. The Examiner rejects claims 21, 34, 41 and 42 as unpatentable over Goldenberg, Schlimok, Crisan, and further in view of U.S. Patent 5,792,456 (Yelton). The Examiner rejects claims 1, 9, 17, 20, 25-27, 29-32, 35-40, 43, and 47 as unpatentable over Ferrari in view of Schlimok and Crisan. The Examiner rejects claims 21, 34, 41, and 42 as unpatentable over Ferrari, Schlimok, Crisan, and further in view of Yelton.

As discussed above, neither Goldenberg nor Ferrari teaches the feature "whereby immunocomplexing of tumor cells within the scope of the surgical intervention inhibits dissemination of tumor cells." Schlimok, Crisan, and Yelton do not remedy this deficiency, and in fact, teach away from the claimed invention.

A reference may teach away from a use when that use would render the result inoperable. *McGinley v. Franklin Sports, Inc.*, 262 F.3d 1339, 1354 [60 USPQ2d 1001] (Fed. Cir. 2001). If one of skill were to apply the teachings of Sclimok and Crisan one of skill would obtain a native antibody, which completely contradicts the intended use and purpose of the antibodies of Goldenberg and Ferrari. Because Goldenberg and Ferrari teach that the labels and microdevices are necessary to obtain the intended effect, one of skill would not negate those teachings by applying Schlimok. Accordingly, Applicants submit that the present invention is not obvious in view of the prior art. Applicants request that the rejection be withdrawn.

6. Non-Statutory Double Patenting

The Examiner provisionally rejects claims 1-5, 7-8, 11-15, 17-19, 22, 25-27, 29-32, 34-35, 38-43, 48 and 49 on the grounds of non-statutory obviousness-type double patenting as being unpatentable over claims 1-5, 9-10, 14, 16-21, and 24-27 of co-pending application no. 10/558,166.

As this rejection is still provisional, there being no allowable subject matter, Applicants ask that the issue be deferred until there is allowable subject matter.

Applicant believes the pending application is in condition for allowance. Applicants earnestly request allowance of all of the claims.

Pursuant to 37 C.F.R. §§ 1.17 and 1.136(a), Applicant(s) respectfully petition(s) for a one (1) month extension of time for filing a reply in connection with the present application, and the required fee of $130.00 is attached hereto.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Leonard R. Svensson Reg. No. 30,330 at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37.C.F.R. §§1.16 or 1.17; particularly, extension of time fees.

Dated: August 17, 2009

Respectfully submitted,

By _____

Leonard R. Svensson
Registration No.: 30,330
BIRCH, STEWART, KOLASCH & BIRCH, LLP
12770 High Bluff Drive
Suite 260
San Diego, California 92130
(858) 792-8855
Attorney for Applicant

Attachment: Antibody Labeling Overview